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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,774	11/08/2000	Alessandro Sette	18623006240	3936

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/709,774	SETTE ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-23,25 and 66-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *66-72* is/are allowed.

6)☒ Claim(s) *18-23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation-in-part of U.S. Application Serial Number 08/305,871, which is a continuation-in-part of U.S. Application Serial Number 08/121,101, and is a continuation-in-part of U.S. Application Serial Number 08/788,822, which claims the benefit of the filing date of provisional applications 60/082,250, 60/101,580 and 60/010,510.

Claims 1-17, 24 and 26-65 have been canceled previously.

New claims 66-72 have been added previously.

Claims 18-23, 25 and 66-72 are currently pending and are the subject of examination in the present Office Action.

1. In view of Applicant's amendment and response filed October 14, 2005, only the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 18-23 and 25 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

It was previously stated: "Base claim 18 recites a polynucleotide encoding a fusion protein comprising at least one pan DR binding peptide comprising SEQ ID NO: 22 and at least one CTL-inducing peptide. The disclosed utility of the claimed invention is to provide peptides for inducing or enhancing an immune response (page 3, line 29 through page 4, line 15 for example). It is well established in the art that HLA class II molecules present peptide antigens to helper (CD4+) T lymphocytes, which specifically recognize the peptide antigen in context of a specific HLA class II molecule. It is also well established that CD8+ cytotoxic T lymphocytes (CTL) recognize specific immunogenic peptides in context of HLA class I molecules. The presently claimed invention consists of a nucleic acid encoding a fusion protein comprising a CTL-stimulating peptide fused to an HLA-DR binding peptide. HLA-DR is a class II molecule. Accordingly, CTL-stimulating peptides bound to the pan-DR binding peptide that is, in turn, bound to HLA-DR cannot be properly presented to CTL. Furthermore, the fusion peptide cannot be processed to separate the CTL peptide from the pan-DR binding peptide and separately present it to CTL in the context of HLA class I. It is well known in the art that MHC class I molecules do not express antigenic peptides obtained via the exogenous pathway, a function exclusive to MHC class II. MHC class I molecules can only express endogenous antigens. See, for example, the illustration from the immunology textbook "Kuby Immunology" (Kuby Immunology, 2000; U on form PTO-892). Additionally, the entire pan-DR binding peptide:CTL peptide construct cannot be presented as an intact peptide in the context of HLA class I because the binding pockets of MHC class I molecules are closed and cannot accommodate peptides of greater than 12 amino acid residues in length.

Accordingly, the claimed invention lacks a well-established utility because CTL peptides are known in the art not to be presented to CTL by HLA class II. The claimed invention lacks a credible asserted utility because one skilled in the art would not find it credible that the CTL peptide could remain attached to the pan-DR binding peptide and be presented in the context of HLA class I or HLA class II to a CTL in order to stimulate the CTL, nor can the CTL peptide be processed according to the exogenous pathway and associated with HLA class I. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001."

3. Applicant's arguments filed October 14, 2005 have been fully considered but they are not persuasive.

Applicant argues that the claimed invention meets the requirements of 35 USC § 101 because the art shows that some antigen presenting cells can process exogenous antigens that can, in turn be expressed in association with MHC class I molecules on the surface of the antigen presenting cell and stimulate cytotoxic T cells. Applicant is reminded, however, that utility must be established and the invention must be enabled at the time the invention is made, i.e., the filing date. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The instant application was filed on November 8, 2000 and it is a continuation-in-part of U.S. Application Serial Number 08/305,871 (filed on September 14, 1994), and is also a continuation-in-part of U.S. Application Serial Number 08/788,822 (January 23, 1997), both of which claim further priority. Brief review of the instantly claimed invention versus these two priority documents reveals that the instantly claimed invention apparently has priority of disclosure to at least 1994. Three of the four references cited by Applicant in the arguments (Heath [2004], Chen [2004] and Alexander [2002] have publication dates that are after the filing date of the instant application and well after the apparent priority date of the claimed invention. Accordingly, these references cannot be relied upon as providing proof of a well-established utility at the time the invention was made because the publications did not exist at that time. Furthermore, as peer-reviewed articles, these reports are assumed to provide new and original findings in the art.

Particularly regarding Heath, the publication discloses that some antigen presenting cells can "cross-present" peptide antigens from other cells from the subject that were apoptotic or phagocytosed by the antigen presenting cells. The Heath reference also discloses DNA vaccination of sequences encoding peptides into muscle cells, which allowed APCs to capture and present those antigens. However, the present specification does not disclose the use of the claimed polynucleotides to transfect cells other than

the APCs for take up of the expressed peptide, the processing thereof and expression of an exogenous peptide sequence in association with MHC class I on the surface of the APC. Accordingly, the instant specification does not show that a utility of the claimed polynucleotide commensurate with the later disclosure of Heath was contemplated.

In regard to Alexander, the publication discloses naked DNA vaccination of muscle tissue for expression of immunogenic peptides, which allowed APCs to capture, process and present antigenic peptides in context of MHC class I. However, again, the present specification does not disclose the use of the claimed polynucleotides to transfect cells other than the APCs for take up of the expressed peptide, the processing thereof and expression of an exogenous peptide sequence in association with MHC class I on the surface of the APC. Accordingly, the instant specification does not show that a utility of the claimed polynucleotide commensurate with the later disclosure of Alexander was contemplated.

The only publication cited by Applicant that predates the date the invention was made is Staerz [1987]. Staerz discloses CTL reactivity to ovalbumin. Applicant asserts that this reference shows that APCs can process soluble antigen for presentation in the context of MHC class I to stimulate T cell reactivity. However, review of the reference shows that while the CTLs were able to react when primed with soluble ovalbumin, they were only able to do so in the presence of CNBr-fragmented ovalbumin (page 450 for example). Staerz also showed that CTL were able to kill EL4 tumor cells that had been transfected with ovalbumin, but not EL4 cells that had taken up exogenous antigen. However, the specification does not disclose the transfection of target cells, only that polynucleotides can be made for expression of the fusion polypeptide for use of the fusion polypeptide in immunization. There is no disclosure of fragmentation of the polypeptide into fragments usable by MHC class I molecules or for the inclusion of enzyme recognition sites. Accordingly, there is not a credible asserted utility in the specification, nor is there an art-recognized utility for the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 18-23 and 25 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

5. Claims 66-72 are allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. PV
Patent Examiner
July 7, 2005

David G Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644